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学位論文題目　Somatosensory evoked magnetic fields following passive movement

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論文内容の要旨

Present thesis including two research works. The first part is somatosensory evoked magnetic fields following passive finger movement, the second part is somatosensory evoked magnetic fields and potentials following passive toe movement in humans. In order to compare the somatosensory evoked magnetic fields (SEFs) (averaged MEG) following passive movement with the SEFs following electrical stimulation, they have recorded the SEFs following passive finger movement and the electrical stimulation of the same finger. In the second part of research work, they have recorded SEFs and somatosensory evoked potentials (SEPs) (averaged EEG) simultaneously in study of passive toe movement to compare the SEFs with SEPs.

The SEFs following passive finger movement and electrical stimulation of the same finger was studied in 10 normal subjects. A new device for passive finger movement was developed for this study. The movement condition of finger was monitored by a rotary differential transformer. To avoid magnetic noises, all parts were made by plastics, woods and optic fibers. The finger was moved approximately 20 degree, and its angular velocity was approximately 525-530 degree/sec. The external trigger was set off by a photometer using laser beam. The electrical stimulus was a constant current square wave pulse delivered transcutaneously to the area between the proximal and distal joint of the left middle finger. The SEFs were measured with dual 37-channel biomagnetometers (Magnes, Biomagnetic Technologies Inc., San Diego, CA). Magnetic resonance imaging (MRI) scans (Shimadzu Magnex 150XT 1.5T) were obtained for all subjects.

Four main components were identified in SEFs recorded at the hemisphere contralateral to the moved finger: 1M(P), 2M(P), 3M(P) and 4M(P). One component, 4M(PI), was identified in SEFs recorded at the hemisphere ipsilateral to the moved finger. The M, P and I stand for magnetic fields, passive movement and ipsilateral, respectively. Isocontour maps of those main responses to passive finger movement showed clear and simple polarity – reversal fields which indicated the single equivalent current dipole (ECD). The 1M(P) was clearly identified only in 3 subjects and was smaller than other components in amplitude, its latency was about 19.4 ms. The ECD of 1M(P) were located around the finger area of primary sensorimotor cortex and oriented either posteriorly or anteriorly. The 2M(P) and 3M(P) were usually combined as one large deflection with two peaks, the duration of this deflection was around 20- 40 ms. The latency of 2M(P) was 46 ms, and the latency of 3M(P) was 70 ms. The ECDs of 2M(P) and 3M(P) were located around the finger area of sensorimotor cortex and both oriented posteriorly. The 4M(P) has large inter-individual difference in terms of amplitude and latency. The ECD of 4M(P) was also located around the finger area of primary sensorimotor cortex, and oriented anteriorly. The 4M(PI), the main component recorded from the hemisphere ipsilateral to the moved finger, was located in the upper bank of Sylvian fissure, probably the secondary sensory cortex (SII). Five components, 1M(E), 2M(E), 3M(E), 4M(E) and 4M(EI), corresponding to 1M(P), 2M(P), 3M(P), 4M(P) and 4M(PI), were identified following electrical stimulation of the same finger. However, SEFs following passive movement was clearly different from SEFs following electrical stimulation, in terms of waveforms and source locations. The differences can be summarized as follows: (1) The 1M(P) was absent or very small, but the 1M(E) was clearly identified in all subjects. The dipole orientation of 1M(P) was either anterior or posterior, but the dipole orientation of 1M(E) was constantly anterior. The peak latency of the 1M(P) was 2 - 3 ms shorter than that of the 1M(E). (2) The 2M(P) and 3M(P) were significantly larger than the 2M(E) and 3M(E) in amplitude and dipole moment ($P < 0.01$). The 2M(P) and 3M(P) appeared to be one large deflection with two peaks, but the 2M(E) and 3M(E) were clearly separated in all subjects. The peak latencies of the 2M(P) and 3M(P) were significantly longer than those of the 2M(E) and 3M(E) ($p < 0.01$). (3) The ECD of 4M(P) was located in the finger area of SI, but that of the 4M(E) was located in SII. Therefore, the Z location of 4M(P) was significantly higher than that of the 4M(E) ($P<0.01$).

The SEFs and SEPs following passive toe movement were studied in 10 normal subjects. The second toe was moved upwards approximately 20 °, and its angular velocity was approximately 435 degree/sec. To record the SEPs, five exploring electrodes were placed at the Fz, Cz, Pz, C3 and C4 sites. The device and other methods are same as the first part of the study.

Four components, 1M, 2M, 3M and 4M, were identified, whose mean peak latencies were approximately 35 ms, 46 ms, 62 ms and 87 ms, respectively. The 1M and 2M were relatively small in amplitude. The 3M and 4M components appeared to be merged as one deflection with two peaks in 7 subjects. The isocontour map of the 1M component was similar to that of 2M, and their estimated ECD locations were just around the Cz in all subjects. However, a large inter-individual difference of the isocontour maps of 1M and 2M, particularly 2M, was found. This finding suggested that the location of ECD was stable but its orientation was vary variable between subjects. In contrast, the isocontour maps of 3M and 4M were relatively consistent. The 1M component was generally oriented horizontally to the right hemisphere in all subjects, but was more vertical in 2 subjects. As for anterior-posterior direction, the 1M was oriented anteriorly in 3 subjects but posteriorly in another 4 subjects. The ECDs of 3M and 4M were closely located in general. The MRI indicated that the ECDs of 3M and 4M were located around the foot area of sensorimotor cortex in the left hemisphere and oriented horizontally to the left hemisphere in all subjects. Equivalent current dipoles (ECDs) of both 1M and 2M were estimated around SI in the hemisphere contralateral to the movement toe, and were probably generated in area 3a or area 2, which mainly receive inputs ascending through muscle and joint afferents. The third and fourth components, 3M and 4M, appeared to be a single large longduration component with two peaks. Since the 3M and 4M components were significantly larger than the 1M and 2M components in amplitude and their ECD location was significantly superior to that of 1M and 2M, we suspected that they were generated in different sites from those of 1M and 2M, probably area 3b or area 4. The variation of first component of SEPs, 1E, could be accounted for by the variation of the orientation of ECD of the 1M component.

In conclusion, the SEFs following passive finger movement was different from the SEFs following electrical stimulation of the same finger in terms of waveforms, isocontour maps, ECD location and orientation. 1M(P) was probably generated in area 3a or 2 of SI, but the 1M(E) was probably generated in area 3b. 2M(P) and 3M(P) were considered to be generated in area 4 and/or 3b, and their activities have temporal overlapping. The 4M(P) was generated in SI, but 4M(E) was generated in SII, however, both 4M(PI) and 4M(EI) were both generated in SII of ipsilateral hemisphere.

## 論文の審査結果の要旨

向敬君の博士論文は受動的な手指及び足指の伸展によって誘発される大脳皮質体性感覚野の活動を脳磁計によって計測し、電気刺激による脳磁場記録や誘発電位による記録と比較・解析したものである。

従来、皮膚の電気刺激や機械的刺激による皮質誘発電位は数多く研究されてきたが、深部感覚の刺激である受動的関節伸展によって誘発される大脳皮質の活動に関する研究は、技術的困難のためにあまりなされてこなかった。この問題に関して、今回の研究において向君らの研究グループでは、巧妙な実験セットを開発して、指に対する同じ振幅・同じ速度の素速い伸展運動を繰り返して与え、またその刺激開始の時刻を正確に電気信号として検出することを可能にし、それによって誘発される脳磁場活動を記録し、発生源を同定することに成功した。その結果、受動的手指伸展運動によって誘発される脳磁場は刺激の反対側の中心後回に誘発され、1M(P), 2M(P), 3M(P), 4M(P)という異なる成分に分けられることが明らかになった。1M(P)は手指刺激で潜時約２０ミリ秒という大変早い反応であるが、検出できるか否か、そしてdipoleの向きにおいて個人差が顕著に見られたため、dipoleが脳の表面に垂直に向いている可能性が考えられ、中心回の底である 3a 野かもしくは表面に露出している２野に起源をもつものと考えられた。2M(P), 3M(P)は中心回付近で検出され、いずれもdipoleが後向きであることから4野または3b野で誘発されているものと考えられた。4M(P)は振幅・潜時ともに個人差が大きかったが、体性感覚野で記録され、dipole は前向きだった。そのほか、刺激と同側の第二次体性感覚野 SII において 4M(PI)という長い潜時の成分も検出された。これに対して皮膚の電気刺激に対しては、同様な潜時で 1M(E), 2M(E), 3M(E), 4M(E)と 4M(EI)という成分が記録されたが、波形や起源に違いが見られ、受動的刺激とは異なる上行性経路をたどるものと考えられた。受動的足指刺激に対しては誘発される脳磁場と電場を比較解析した結果、1M, 2M, 3M, 4M の４種の成分が記録され、1M、2M は 3a 野か２野の下肢の領域、3M と 4M は 3b か 4 野の下肢領域で誘発されること、そしてこれらは電場で記録される成分によく対応することが確認された。

これらの結果は時間解像度と空間解像度に優れた脳磁計の利点をうまく活用して、深部感覚の知覚に関与する可能性のある大脳皮質領域を同定した重要な基礎的研究であり、高く評価できる。また論文の内容も既に向君が筆頭著者である２編の論文として発表されている。以上の理由で、この論文は博士の学位論文として十分な内容を持つ、と審査員全員の意見が一致した。

さらに、発表に引き続き、４人の審査委員が向君と質疑応答を行い、実験結果及びその背景となる関連分野に関する知識と考察力を質した。その結果、これらの内容について十分な理解がなされており、博士として十分な学力があるものと判断された。また学位論文は英語で書かれ、さらに既に筆頭著者の論文として２編の論文が国際誌に掲載されていることから十分な英語力を有すると判断した。